Primary Varicella in an Immunocompetent Adult

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ABSTRACT

Primary varicella zoster infection in adults and immunocompromised persons may result in serious complications. For this reason, a speedy and accurate diagnosis is essential to prevent life-threatening sequelae. Primary varicella presents as a vesicular exanthem with fevers and other constitutional symptoms. The differential diagnosis of primary varicella zoster infection comprises several other important entities, including smallpox infection, which should be considered before definitive diagnosis of varicella is made. Here, the authors describe an immunocompetent adult with primary varicella infection and review the literature on its clinical presentation and treatment.
(*J Clin Aesthetic Dermatol.* 2009;2(8):36–38.)

Varicella, or chicken pox, is a highly contagious infection characterized by an exanthematous vesicular rash and systemic symptoms. Newly infected adults and immunocompromised individuals may have a more severe presentation and serious complications. Meyer et al found that during the 25 years before the varicella vaccine was licensed in 1995, rates of death for which varicella was the underlying cause fluctuated from 47 to 138 deaths per year, or 0.29 to 0.46 death per one million population. From 1990 through 1994, most deaths (54 percent) were among adults 20 years of age or older.[1,2] Since the inception of varicella zoster virus (VZV) vaccination, age-adjusted mortality rates where varicella was listed as the underlying cause dropped by 66 percent.[2] Furthermore, infection during pregnancy may lead to numerous detrimental consequences for the fetus and newborn.[3,4]

Here, we describe a case of primary VZV (pVZV) in a healthy young woman, and discuss the diagnosis and management of pVZV in affected individuals.

CASE

A previously healthy 33-year-old woman presented with a four-day history of a disseminated vesicular follicular-based eruption resembling "dew drops on a rose petal." Vesicles were in different stages of evolution and were itchy and tender (Figure 1). For two days preceding the rash, she had severe headaches, myalgias, high fevers, generalized malaise, fatigue, sweats, a sore throat, and tenderness to palpation in the right upper quadrant. She had no nuchal rigidity or respiratory complaints. She never had chicken pox as a child nor received vaccination against varicella. A blood smear obtained upon admission showed 21 percent atypical lymphocytes. Liver function tests showed a mild transaminitis. Skin biopsy showed acute pustular folliculitis (Figures 2A, B, and C), with positive staining for the VZV antigen (Figures 2C, D, and E). There was no VZV DNA in the cerebrospinal fluid by polymerase chain reaction analysis. The patient had no evidence of an underlying immunocompromised state. She had a negative human immunodeficiency virus test and did not report an increase in the number of infections over the past several years. She was not pregnant, and her previous age-appropriate health screens were normal. The patient's exanthem and constitutional symptoms resolved without antiviral medications, and she had no complications at a six months follow up.

DISCUSSION

Primary varicella zoster virus will continue to occur in young unvaccinated adults without a history of childhood infection. Because pVZV infection tends to be more severe in adult patients, they are at a greater risk for serious complications. Since some of the young adult patients are

DISCLOSURE: Dr. Izikson and Ms. Lilly report no conflicts of interest.
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FIGURE 1. Clinical examination revealed a vesicular eruption resembling "dew drops on a rose petal" (A = nose; B = palm; and C = abdomen) with vesicles in different stages of evolution (A).

women of childbearing age, as is the case with our patient, it is important to beware that infection during the first two trimesters of pregnancy may cause severe congenital malformations, while infection in the third trimester may cause disseminated and complicated varicella in the newborn.[3,4] Accordingly, vaccination of all women of childbearing age without prior immunity may be beneficial. All such women, especially those contemplating pregnancy, should be routinely screened for varicella antibodies and immunized when necessary.

VZV (HHV-3) is a herpes virus endemic in humans.[5–7] It affects both sexes and all races. Primary infections usually occur in childhood and more often in late winter and early spring.[8] The VZV incubation period ranges from 10 to 21 days, and patients are infectious from two days before the vesicular rash until vesicles have crusted. VZV is transmitted by inhalation of infectious droplets or contact with lesions, and infects epithelial cells,[9] where it replicates to cause viremia. Patients seroconvert after infection. VZV subsequently lies dormant in ganglionic neurons and can cause herpes zoster (shingles) on reactivation in 10 to 30 percent of the population.[7,9]

Symptoms of pVZV begin with a rash, low-grade fever, and malaise, all of which are more severe in adults. Some patients develop a prodrome before the vesicular rash.[8] Skin lesions progress over hours from erythematous macules and papules to vesicles and then to crusted scabs. As a result, vesicles at various stages of evolution are found on the skin. New batches of lesions appear every few days, starting on the face and trunk, and spread to the extremities in a so-called "centripetal spread." Adults tend to have more numerous, larger lesions, while immunocompromised individuals often develop lesions with more prominent hemorrhagic bases that take longer to heal.[8]

Diagnosis of VZV can be made from clinical signs and history. A Tzanck test made from the blister roof and contents may reveal multinucleated giant cells with intranuclear inclusion bodies. Occasionally, definitive diagnosis may require histological, immunopathological, serological, and microbiological analyses, or direct fluorescent antibody testing of blister contents. In our patient, histopathology revealed classic findings of VZV infection, and immunostaining showed the presence of VZV infection in the cells.

The differential diagnosis of vesicular exanthemata with fevers and systemic complaints comprises many important entities, both in adults and in children. Smallpox is the most serious consideration. Smallpox, or variola infection, has become a greater concern due to threats of bioterrorism, and presents with larger lesions in the same stage of evolution. When untreated, its mortality approaches 30 percent.[10] Disseminated vaccinia, which may develop after smallpox vaccination in military or healthcare personnel, and eczema herpeticum, or disseminated herpes simplex virus infection in patients with atopic dermatitis, may also resemble primary varicella.

Disseminated vesiculopapular lesions also occur with coxsackievirus and echovirus infection, in rickettsialpox, and in atypical measles. Other important considerations include meningococcal or gonococcal infection, bullous vasculitis, infectious endocarditis, acute generalized exanthematous pustulosis (a type of drug reaction), pustular psoriasis, and Mucha-Habermann disease.

In caring for patients with varicella, it is important to evaluate them for any signs of complications. Primary varicella zoster virus infection in immunocompetent adults may result in such serious sequelae as secondary varicella pneumonia in 20 percent of patients, bacterial skin infection, acute cerebellar ataxia, meningeal inflammation, encephalitis, unifocal large vessel vascular damage that may lead to stroke, myocarditis, nephritis, arthritis, and hepatitis.[7]

Antiviral therapy with acyclovir may be helpful.[5,6] Since our patient presented four days after the onset of exanthem, without pneumonitis or meningoencephalitis, she received only supportive treatment with a good outcome. Antiviral treatment is generally recommended within the first four days of the cutaneous eruption and for severe cases, including adults, pregnant women, and immunocompromised individuals.[5] Three double-blind, placebo-controlled trials in children and one in adults showed statistically significant reductions in the duration of fever, constitutional illness, and time-to-cutaneous healing with therapy.[6] Aspirin should be avoided due to the risk of Reye's syndrome in children, but acetaminophen can be used safely as an antipyretic.

To prevent further spread of VZV, patients should be isolated and caregivers should use gowns, gloves, and masks.[8] It is important to limit the exposure of infected individuals to pregnant women and those with

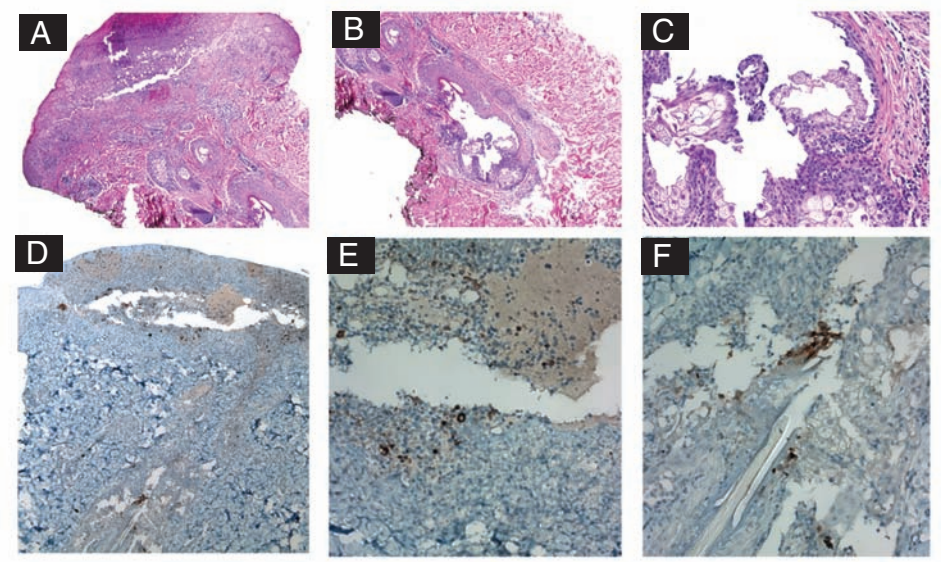

FIGURE 2. Histopathological examination of a skin biopsy revealed a vesicular necrotizing folliculitis: an epidermal vesicle with prominent epidermal necrosis and a mixed infiltrate (A = 5x), as well as acute folliculitis with a mixed infiltrate surrounding the hair follicle and the sebaceous gland (B = 5x; C = 20x). VZV antigen expression was positive in epidermal (D = 5x and E = 20x) and follicular keratinocytes (F = 20x).

compromised immune systems. Supportive measures for infected patients should include daily bathing, soaks, fingernail cropping, oral antihistamines, and wet compresses. These measures will decrease itching, diminish the likelihood of residual pitted scars, and prevent secondary bacterial skin infections.

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